MULTIPLE MYELOMA Research Foundation

Management of Patients Who Have Relapsed After One to Three Prior Lines of Therapy

July 13, 2022

1

Tech Support

1-719-234-7952

2

3

Resources

- Resource tab includes
  - Speaker bios
  - Copy of the slide presentation
  - Exhibit Hall

Submit your questions throughout the program!

MM RF

4

MMRF Research Initiatives

MULTIPLE MYELOMA Research Consortium

CoMMpass Study℠

MMRF CureCloud™

For more information, please visit themmrf.org

5

Speakers

Larry D. Anderson, Jr., MD, PhD
UT Southwestern Medical Center
Simmons Comprehensive Cancer Center
Dallas, Texas

Faith E. Davies, MBBCh, MD
Perlmutter Cancer Center
New York University/Langone Health
New York, New York

Pamela Jones
Patient Advocate

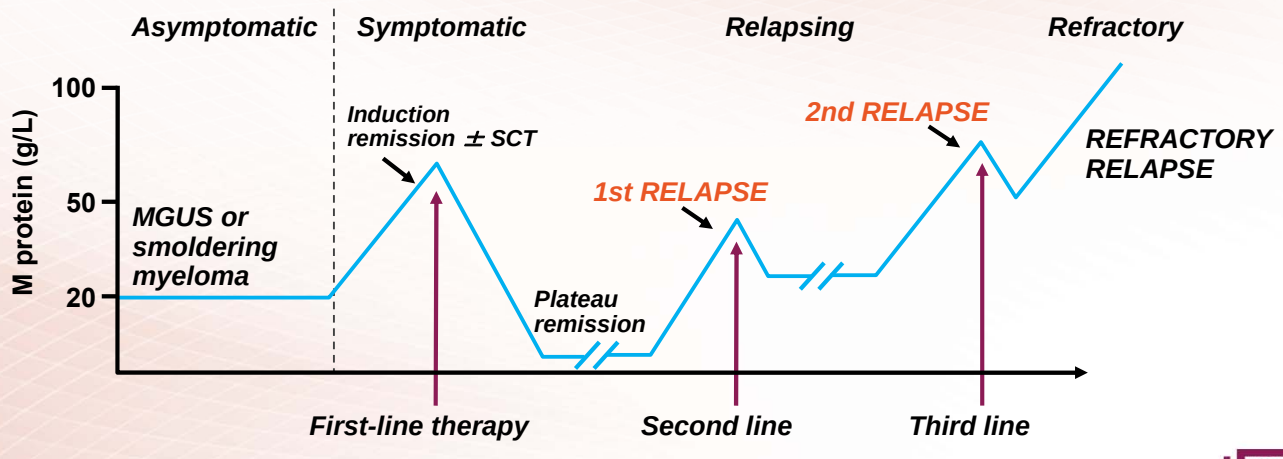
6

Treatment Options and Considerations for Multiple Myeloma Patients at Relapse

Faith E. Davies, MBBCh, MD
Perlmutter Cancer Center
New York University/Langone Health
New York, New York

7

Multiple Myeloma Is a Marathon, Not a Sprint



Adapted from Borrello I. *Leuk Res*. 2012;36 Suppl. 1:S3.

8

Definitions: What is relapsed/refractory disease and a line of therapy?

- ***Relapsed:*** recurrence (reappearance of disease) after a response to therapy
- ***Refractory:*** progression despite ongoing therapy
- ***Progression:*** change in M protein/light chain values
- ***Line of therapy:*** change in treatment due to either progression of disease or unmanageable side effects
  - **Note:** initial (or induction) therapy + stem cell transplant + consolidation/maintenance therapy = 1 line of therapy

9

Biochemical Relapse or Clinical Relapse

Biochemical

- Patients with asymptomatic rise in blood or urine M protein, free light chains, or plasma cells

→ **Timing of therapy initiation/escalation dependent on numerous factors**

Clinical

- Based on direct indicators of increasing disease and/or end-organ dysfunction

→ **Mandates immediate initiation/escalation of therapy**

10

Choosing Therapy for First or Second Relapse

Choices are broadest and guided by

- Disease biology
- Nature of relapse
- Patient preference

Factors to consider

- Prior autologous stem cell transplant
- Prior therapies
- Aggressiveness of relapse
- Comorbidities
- Psychosocial issues
- Access to care

11

Options for Relapsed/Refractory Disease Continue to Increase

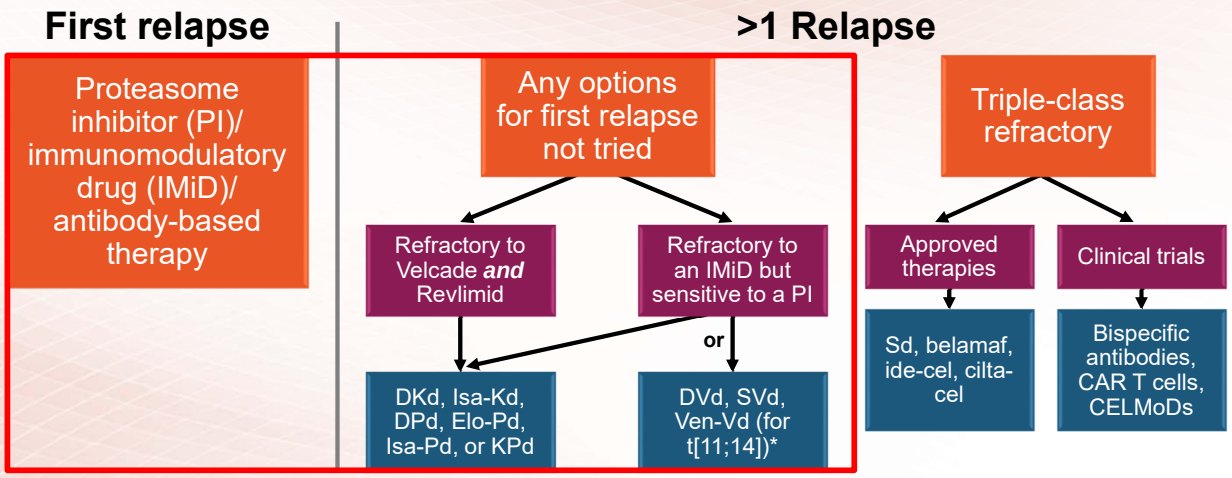
IMiDs	Proteasome inhibitors	Chemotherapy anthracyclines	Chemotherapy alkylators	Steroids	Novel mechanisms of action	mAbs	Cellular therapy
Thalomid (thalidomide)	Velcade (bortezomib)	Adriamycin	Cytoxan (cyclophosphamide)	Dexamethasone	XPOVIO (selinexor)	Empliciti (elotuzumab)	Abecma (idecabtagene vicleucel)
Revlimid (lenalidomide)	Kyprolis (carfilzomib)	Doxil (liposomal doxorubicin)	Bendamustine	Prednisone	Venclexta (venetoclax)*	Darzalex (daratumumab)	Carvykti (ciltacabtagene autoleucel)
Pomalyst (pomalidomide)	Ninlaro (ixazomib)		Melphalan		~~Farydak (Panobinostat)~~†	Sarclisa (isatuximab)	
					~~Pepaxto (melflufen)~~†	Blenrep (belantamab mafodotin)‡	

*Not yet FDA-approved for patients with multiple myeloma; †Withdrawn from the US market in 2021; ‡Antibody-drug conjugate

New formulations, new dosing, and new combinations, too!

12

Treatment Approach

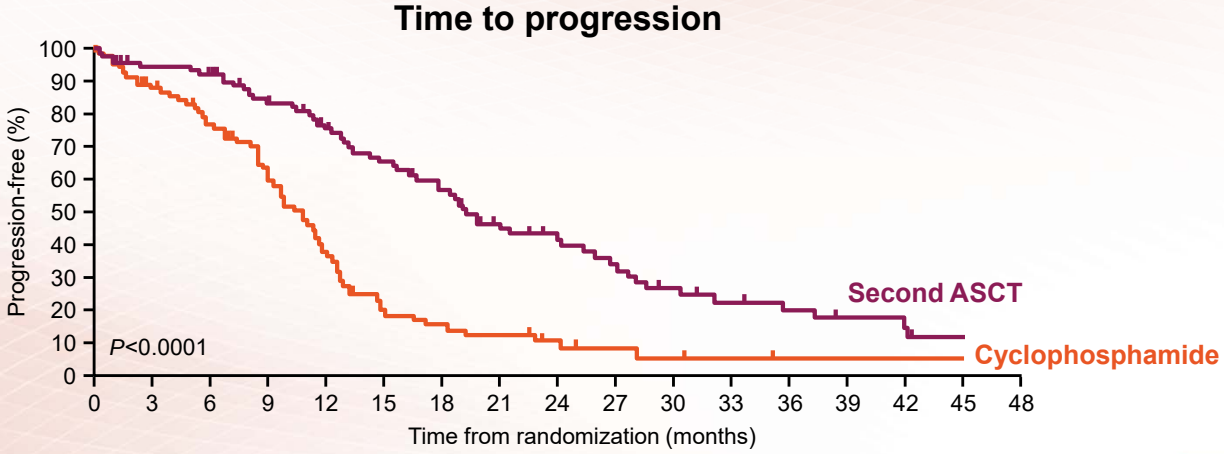


D, daratumumab (Darzalex); K, carfilzomib (Kyprolis); d, dexamethasone; Isa, isatuximab (Sarclisa); P, pomalidomide (Pomalyst); Elo, elotuzumab (Empliciti); V, bortezomib (Velcade); S, selinexor (Xpovio); Ven, venetoclax (Venclexta); belamaf, belantamab mafodotin (Blenrep); ide-cel, idecabtagene vicleucel (Abecma); cilta-cel, ciltacabtagene autoleucel (Carvykti)

*Not yet approved for use in myeloma patients

13

Second ASCT an Option for Early Relapse



Cook G et al. *Lancet Oncol*. 2014;15:874.

14

Proteasome Inhibitor–Based Regimens for Early Relapse

	OPTIMISMM	ASPIRE	TOURMALINE-MM1	BOSTON
Regimens Compared	• Velcade-Pomalyst-dex (VPd) vs Vd	• Kyprolis-Revlimid-dex (KRd) vs Rd	• Ninlaro-Rd (IRd) vs Rd	• XPOVIO-Velcade-dex (XPO-Vd) vs Vd
Median progression-free survival favored:	• VPd: 11 vs 7 months	• KRd: 26 vs 17 months	• IRd: 21 vs 15 months	• XPO-Vd: 14 vs 9 months

15

Important Considerations for Use of Proteasome Inhibitors

Velcade

- Risk of **peripheral neuropathy (PN;** numbness, tingling, burning sensations and/or pain due to nerve damage)
  - Avoid in patients with severe existing PN
  - Reduced with subcutaneous once-weekly dosing
- High risk of **shingles**
  - Use appropriate vaccination
- No dose adjustment for kidney issues; but adjust for liver issues

IV infusion or SC injection

Kyprolis

- Less **PN** than Velcade
- High risk of **shingles**
  - Use appropriate vaccination
- Monitor for **heart, lung, and kidney side effects**
  - Use with caution in older patients with cardiovascular risk factors
- High blood pressure
- No dose adjustment for kidney issues; but adjust for liver issues

IV infusion and weekly dosing

Ninlaro

- Less **PN** than Velcade
- High risk of **shingles**
  - Use appropriate vaccination
- Monitor for rashes and **gastrointestinal (GI)** side effects
  - GI effects occur early
- Needs to be taken at least 1 hour before or 2 hours after a meal

Once weekly pill

*Do not take any supplements without consulting with your doctor.

16

Important Considerations for Use of Immunomodulatory Drugs

Revlimid*

- **Rash**
  - Consider antihistamines
- **Diarrhea**
  - Consider bile acid sequestrants
- Risk of **blood clots**
- Risk of second primary **malignancies**
- Dose adjustment based on kidney function

Once-a-day pill

Pomalyst*

- **Low blood counts**
- Less **rash** than Revlimid
- Risk of second primary **malignancies**
- Risk of **blood clots**

Once-a-day pill

*Black box warning.

17

Important Considerations for Use of XPOVIO

Gastrointestinal

Begin prophylactic anti-nausea medications.
Consult with your doctor if nausea, vomiting, or diarrhea occur or persist.

Low sodium (hyponatremia)

Maintain fluid intake.
Salt tabs

Fatigue

Stay hydrated and active.

Low blood counts (cytopenias)

Report signs of bleeding right away.
Report signs of fatigue or shortness of breath.

Chari A et al. Manuscript under preparation.

18

Proteasome Inhibitor–Based Regimens for Early Relapse

	OPTIMISMM	ASPIRE	TOURMALINE-MM1	BOSTON
Regimens compared	• Velcade-Pomalyst-dex (VPd) vs Vd	• Kyprolis-Revlimid-dex (KRd) vs Rd	• Ninlaro-Rd (IRd) vs Rd	• XPOVIO-Velcade-dex (XPO-Vd) vs Vd
Median progression-free survival favored	• VPd: 11 vs 7 months	• KRd: 26 vs 17 months	• IRd: 21 vs 15 months	• XPO-Vd: 14 vs 9 months
Clinical considerations	• Consider for relapse on Revlimid • VPd associated with more low blood counts, infections, and neuropathy than Pd	• KRd associated with more upper respiratory infections and high blood pressure than Rd	• IRd an oral regimen • Gastrointestinal toxicities and rashes • Lower incidence of peripheral neuropathy	• XPO-Vd associated with low platelet counts and fatigue with triplet, but less neuropathy than the Vd

19

Monoclonal Antibody–Based Regimens at Relapse

Larry D. Anderson, Jr., MD, PhD
UT Southwestern Medical Center
Simmons Comprehensive Cancer Center
Dallas, Texas

20

Monoclonal Antibody–Based Regimens for Early Relapse: Darzalex

	POLLUX	CASTOR	CANDOR	APOLLO
Regimens compared	• Darzalex-Revlimid-dex (DRd) vs Rd	• Darzalex-Velcade-dex (DVd) vs Vd	• Darzalex-Kyprolis-dex (DKd) vs Kd	• Darzalex-Pomalyst-dex (DPd) vs Pd
Median progression-free survival favored	• DRd: Not reached vs 17 months	• DVd: 17 vs 7 months	• DKd: Not reached vs 16 months	• DPd: 12 vs 7 months

21

Important Considerations for Use of Darzalex

Darzalex

- **Infusion reactions**
  - Less with SC use
- Risk of **shingles**
  - Use appropriate vaccination

IV infusion or SC injection

22

Monoclonal Antibody–Based Regimens for Early Relapse: Darzalex

	POLLUX	CASTOR	CANDOR	APOLLO
Regimens compared	• Darzalex-Revlimid-dex (DRd) vs Rd	• Darzalex-Velcade-dex (DVd) vs Vd	• Darzalex-Kyprolis-dex (DKd) vs Kd	• Darzalex-Pomalyst-dex (DPd) vs Pd
Median progression-free survival favored	• DRd: Not reached vs 17 months	• DVd: 17 vs 7 months	• DKd: Not reached vs 16 months	• DPd: 12 vs 7 months
Clinical consider-ations	• Consider for relapses from Revlimid or Velcade maintenance • DRd associated with more upper respiratory infections, low blood white blood cell counts, and diarrhea	• Consider for patients who are Revlimid-refractory without significant neuropathy • DVd associated with more low blood cell counts	• Consider for younger, fit patients who are double-refractory to Revlimid and Velcade • DKd associated with more respiratory infections • Sever side effects (possibly fatal) in intermediate fit patients 65 and older	• Consider in patients who are double-refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro) • Severe low white blood cell counts

23

Monoclonal Antibody–Based Regimens for Early Relapse: Sarclisa and Empliciti

	ELOQUENT-2	ELOQUENT-3	ICARIA-MM	IKEMA
Regimens compared	• Empliciti-Revlimid-dex vs Rd	• Empliciti-Pomalyst-dex vs Pd	• Sarclisa-Pomalyst-dex vs Pd	• Sarclisa-Kyprolis-dex vs Kd
Median progression-free survival favored:	• Empliciti-Rd: 19 vs 15 months	• Empliciti-Pd: 10 vs 5 mos	• Sarclisa-Pd: 12 vs 7 mos	• Sarclisa-Kd: Not reached vs 19 mos

24

Important Considerations for Use of Monoclonal Antibodies

Sarclisa

- **Infusion reactions**
- Risk of **shingles**
  - Use appropriate vaccination

IV infusion

Empliciti

- Lower rate of **infusion reactions** than Darzalex or Sarclisa
- Risk of **shingles**
  - Use appropriate vaccination

IV infusion

25

Monoclonal Antibody–Based Regimens for Early Relapse: Sarclisa and Empliciti

	ELOQUENT-2	ELOQUENT-3	ICARIA-MM	IKEMA
Regimens compared	• Empliciti-Revlimid-dex vs Rd	• Empliciti-Pomalyst-dex vs Pd	• Sarclisa-Pomalyst-dex vs Pd	• Sarclisa-Kyprolis-dex vs Kd
Median progression-free survival favored	• Empliciti-Rd: 19 vs 15 months	• Empliciti-Pd: 10 vs 5 mos	• Sarclisa-Pd: 12 vs 7 mos	• Sarclisa-Kd: Not reached vs 19 mos
Clinical consider-ations	• Consider for non-Revlimid refractory, frailer patients • Overall survival benefit with Empliciti-Rd • Empliciti-Rd associated with more infections	• Consider for patients refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro)	• Consider for patients refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro) • Sarclisa-Pd associated with severe low white blood cell counts, more dose reductions, upper respiratory infections, and diarrhea	• Consider for patients refractory to Revlimid and Velcade • Sarclisa-Kd associated with higher MRD negativity rates • Sarclisa-Kd associated with severe respiratory infections

26

Current and Emerging Therapies for Relapsed/Refractory Multiple Myeloma

Current therapies

Antibody-drug conjugates

- Blenrep
- Targets BCMA
- A monoclonal antibody conjugated by a protease-resistant linked to a microtubule-disrupting agent

Chimeric antigen receptor (CAR) T cells

- Abecma and Carvykti
- Targets BCMA
- Genetically modified autologous T cells that attack myeloma cells

Emerging therapies

Bispecific antibodies

- Teclistamab, elranatamab, and others
- Targets BCMA on myeloma cells and CD3 on T cells
- Redirects T cells to myeloma cells

Cereblon E3 ligase modulators (CELMoDs)

- Iberdomide
- Targets cereblon
- Enhances tumoricidal and immune-stimulatory effects compared with immunomodulatory agents

Small molecule inhibitors

- Venetoclax
- Targets Bcl-2
- Induces multiple myeloma cell apoptosis

27

Summary

- **We now have many different options for relapsed myeloma depending on patient and myeloma factors at relapse.**
- **Therapy choices will depend on teamwork between physician and patient and caregivers and are based on multiple decision points.**
- **Combinations of proteasome inhibitors with either immunomodulatory drugs or selinexor improve progression-free survival.**
- **We have three different monoclonal antibodies that improve progression-free survival when added to other standard therapies without significantly increasing side effects.**
- **In general, three-drug combinations are going to work better than two drugs.**
- **Many other exciting immunotherapy options are in trials and look very promising.**

28

Patient Experience

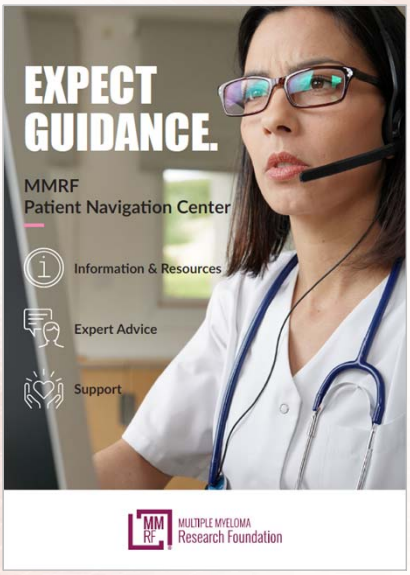
29

Questions & Answers

30

31

MMRF Patient Resources



MMRF Patient Navigation Center

You and your care team will have many decisions to make along your treatment journey. The Patient Navigation Center is a space for multiple myeloma patients and their caregivers to connect with patient navigators — who are professionals specializing in oncology — for guidance, information, and support. You can connect with a patient navigator via phone, or email. Whatever questions you may have, our patient navigators are here to help.

MMRF Patient Navigators include:
- Grace Allison, RN, BSN, OCN, RN-BC
- Brittany Hartmann, RN-BSN
- Erin Mensching, RN-BSN, OCN

THE RIGHT TRACK

Get on the right track for you

The MMRF's Right Track program puts you on the path to the best results for you.

Right Team
Access experts and centers that have extensive experience treating multiple myeloma.

Right Tests
Get the information, tests, and precise diagnoses to make the right treatment decisions.

Right Treatment
Work with your team to consider the best treatment plan and identify clinical trials that are right for you.

Contact the Patient Navigation Center Today

Looking for guidance? We're here to help.
Monday – Friday | 9:00AM – 7:00PM ET
Phone: 1-888-841-MMRF (6673) Online: TheMMRF.org/PatientNavigationCenter
Email: patientnavigator@themmrf.org

Supported By
Adaptive · AMGEN · Bristol Myers Squibb · cure · Genentech · janssen · sanofi · Takeda | ONCOLOGY

32

Myeloma Mentors®

Myeloma Mentors® allows patients and caregivers the opportunity to connect with trained mentors. This is a phone-based program offering an opportunity for a patient and/or caregiver to connect one-on-one with a trained patient and/or caregiver mentor to share his or her patient journeys and experiences.

No matter what your disease state—smoldering, newly diagnosed, or relapsed/refractory—our mentors have insights and information that can be beneficial to both patients and their caregivers.

Contact the Patient Navigation Center at 888-841-6673 to be connected to a Myeloma Mentor or to learn more.

33

MMRF Events

Our events are returning live and in-person, and there are so many ways to get involved. Most have a virtual option, too. Join us today!

Endurance Events

5K Walk/Run Events

Independent Events

FIND AN EVENT AND JOIN US: themmrf.org/get-involved/mmrf-events/

34

Upcoming Patient Education Events
Save the Date

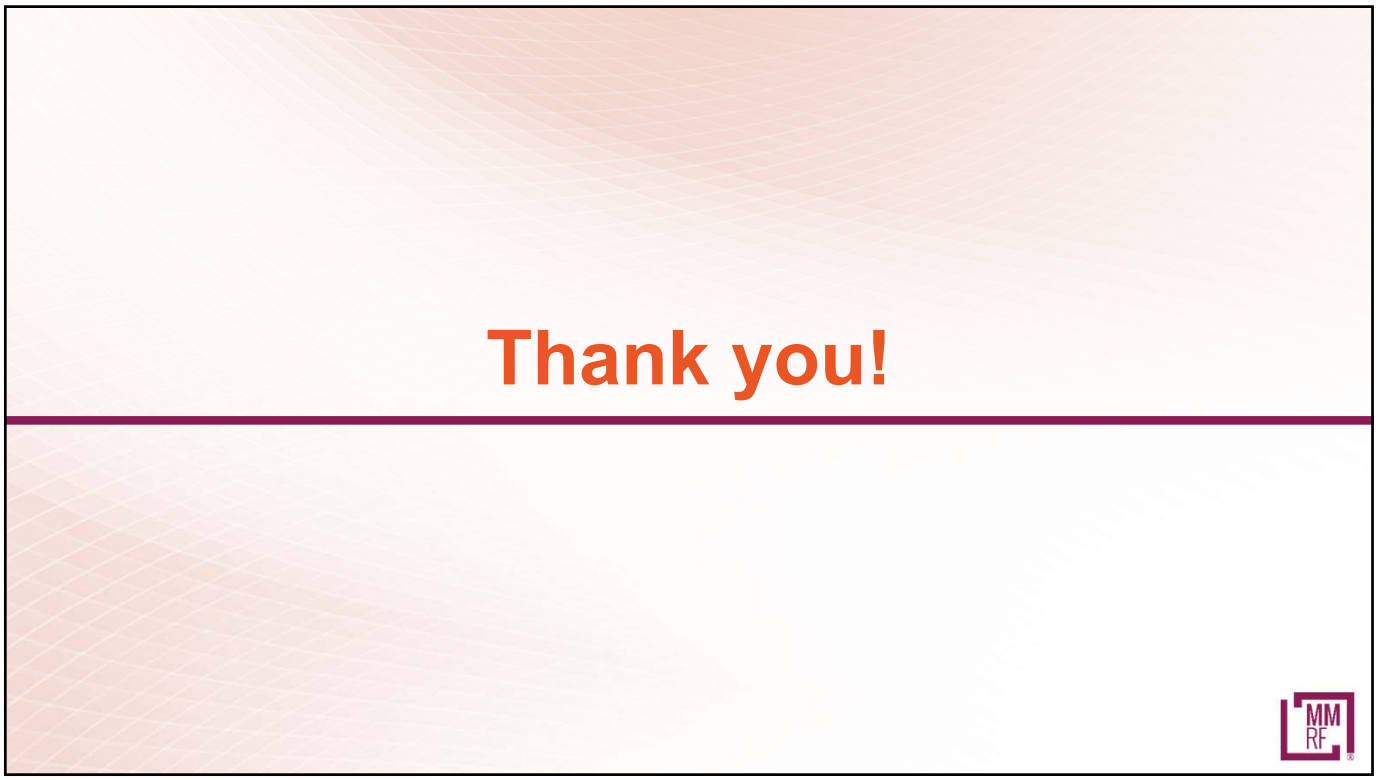
Topic	Date and Time (ET)	Speakers
Facebook Live Session	Wednesday, July 20 at 1:00 PM	Ravi Vij, MD Angela Vickroy, ANP-BC, OCN
Facebook Live Session	Thursday, July 28 at 1:00 PM	Andrew Yee, MD Stephanie Sandford, NP-C, APRN, RN
Patient Webinar— Precursor Conditions	Wednesday, August 17 at 1:00 PM	Sagar Lonial, MD Omar Nadeem, MD
Patient Summit (live and online)	Saturday, August 20 9:00 AM – 2:00 PM St. Louis, Missouri	Ravi Vij, MD—Host
Patient Summit (live and online)	Saturday, October 22 9:00 AM – 2:00 PM Nashville, Tennessee	Jesus Berdeja, MD—Host

For more information or to register,
please visit themmrf.org/resources/education-program

35

Adaptive biotechnologies™
cure 20TH
Genentech
A Member of the Roche Group
GSK
janssen
Karyopharm® Therapeutics
Takeda ONCOLOGY

36



37